AN 2000:30720176 BIOTECHNO

TI Dichotomy between neurokinin receptor actions in modulating allergic airway responses in an animal model of helper T cell type 2 cytokine-associated inflammation

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DT Journal; Article

CY United States

LA English

SL English

AB Neurokinins (NKs), which include substance P (SP) and neurokinin A (NKA), act through NK-1 and NK-2 receptors. There is considerable evidence of interaction between the neurogenic and the immune systems, and NKs are candidates for mediating such interactions. We hypothesized that selective inhibition of pulmonary NK-1 or NK-2 receptors may modulate immune responses so as to prevent the development of allergic airway responses in the atopic BN rat sensitized to ovalbumin (OA). To address this hypothesis, we have validated our animal model by showing that NK-1 and NK-2 receptors are expressed in the lungs, and that SP is released in the airways after allergen challenge. The selective NK-1 (CP-99,994) or NK-2 (SR-48968) antagonists before allergen challenge failed to reduce the allergic early airway responses. In contrast, both neurokinin antagonists decreased allergen-induced late airway responses in OA-challenged animals. However, only the NK-2 antagonist decreased the eosinophil numbers in the bronchoalveolar lavage (BAL). Likewise, the NK-2, but not NK-1, antagonist decreased both Th1 (INF-γ) and Th2 (IL-4 and -5) cytokine expression in BAL cells by in situ hybridization. These results provide initial in vivo evidence linking neurokinins to the regulation of cytokine expression in cells without discrimination as to their phenotype. We conclude that there is a dichotomy between NK receptors in the modulation of the allergic airway inflammation, which has important implications for future therapeutic strategies for asthma using the NK antagonists.

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CT *immunomodulation; *allergic asthma; *protein expression; *tachykinin receptor; *substance P; *neurokinin 1 receptor; *neurokinin 2 receptor; *cyclophilin; airway dynamics; receptor binding; lung lavage; . . . rat; animal model; controlled study; animal tissue; animal cell; article; priority journal; tachykinin receptor antagonist; 3 (2 methoxybenzylamino) 2 phenylpiperidine; saredutant

RN (substance P) 33507-63-0; (cyclophilin) 126043-36-5; (3 (2 methoxybenzylamino) 2 phenylpiperidine) 136982-36-0; (saredutant) 142001-63-6

CN Drug Trade Name: cp 99994; sr 48968

AN 2002:36140454 BIOTECHNO
TI Advances in allergy management
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SO Allergy: European Journal of Allergy and Clinical Immunology, Supplement, (2002), 57/75 (29-36), 70 reference(s)
CODEN: ALSUET ISSN: 0108-1675
DT Journal; Article
CY Denmark
LA English
SL English
AB Our understanding of the pathophysiology of allergy has moved to the molecular level, while study of epidemiology and genetics has revealed risks of developing allergies based on environmental and genetic profiles, and pharmacoeconomic data have enabled accurate measurement of the immense burden of allergic disease. These advances in allergy research have affected its management, particularly the search for new antiallergy therapies. New therapies should intervene in the systemic allergy inflammatory cascade and provide clinical efficacy that extends to multiple allergic disease states. In addition, these new therapies should present no additional safety issues, offer improvements over existing therapies, and have an impact on disease-impaired quality of life. In vitro studies show that desloratadine, a new, once-daily, nonsedating, selective histamine H.sub.1-receptor antagonist, blocks the systemic allergy cascade at multiple points. Desloratadine 5 mg once daily relieves the symptoms of chronic idiopathic urticaria and of both seasonal (SAR) and perennial allergic rhinitis. In patients with concomitant asthma and SAR, asthma symptoms are relieved and β.sub.2-agonist medication use is decreased by desloratadine. Unlike many other second-generation histamine H.sub.1-receptor antagonists, desloratadine provides the added benefit of efficacy against nasal obstruction in SAR. Desloratadine improves quality of life by decreasing the impact of allergic symptoms on sleep and on daily activities.
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AB Our understanding of the pathophysiology of allergy has moved to the molecular level, while study of epidemiology and genetics has revealed risks of developing allergies based on environmental and genetic profiles, and pharmacoeconomic data have enabled accurate measurement of the immense burden of allergic disease. These advances in allergy research have affected its management, particularly the search for new antiallergy therapies. New therapies should intervene in the systemic allergy inflammatory cascade and provide clinical efficacy that extends to multiple allergic disease states. In addition, these new therapies should present no additional safety issues, offer improvements over existing therapies, and have. . . quality of life. In vitro studies show that desloratadine, a new, once-daily, nonsedating, selective histamine H.sub.1-receptor antagonist, blocks the systemic allergy cascade at multiple points. Desloratadine 5 mg once daily relieves the symptoms of chronic idiopathic urticaria and of both seasonal (SAR) and perennial allergic rhinitis. In patients with concomitant asthma and SAR, asthma symptoms are relieved and β.sub.2-agonist medication use is decreased by desloratadine.. . . the added benefit of efficacy against nasal obstruction in SAR. Desloratadine improves quality of life by decreasing the impact of allergic symptoms on sleep and on daily activities.
CT *allergy; *desloratadine; *histamine H1 receptor antagonist; pathophysiology; epidemiological data; risk assessment; treatment outcome; drug efficacy; drug indication; human; article; priority journal;. . . omalizumab; altrakincept; mepolizumab; zafirlukast; montelukast; 1 [2 [3 (3,4 dichlorophenyl) 1 (3 isopropoxyphenylacetyl) 3 piperidyl]ethyl] 4 phenyl 1 azoniabicyclo[2.2.2]octane chloride;

saredutant; 1 alkyl 2 acetylglycerophosphocholine esterase

RN. . . (montelukast) 151767-02-1, 158966-92-8; (1 [2 [3 (3,4 dichlorophenyl) 1 (3 isopropoxyphenylacetyl) 3 piperidyl]ethyl] 4 phenyl 1 azoniabicyclo[2.2.2]octane chloride) 153050-21-6, 154728-59-3; (saredutant) 142001-63-6

CN Drug Trade Name: xolair; nuvance; accolate; singulair